NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

MANAGEMENT OF OSTEOARTHRITIS OF THE KNEE

GUIDELINES BEING COMPARED

1. **American Academy of Orthopaedic Surgeons (AAOS)**. American Academy of Orthopaedic Surgeons treatment of osteoarthritis of the knee (non-arthroplasty). Rosemont (IL): American Academy of Orthopaedic Surgeons (AAOS); 2008 Dec 6. 263 p. [111 references]
2. **Singapore Ministry of Health (SMOH)**. Osteoarthritis of the knees. Singapore: Singapore Ministry of Health; 2007 May. 51 p. [91 references]

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AREAS OF AGREEMENT AND DIFFERENCE

A direct comparison of the recommendations presented in the above guidelines for the management of osteoarthritis is provided below.

Areas of Agreement

Physical Activity and Weight Loss

The groups agree that weight loss can result in improved knee function, and that overweight patients should be encouraged to lose weight through a combination of dietary modification and exercise. Both groups recommend that patients be encouraged to perform low-impact aerobic exercises as well as quadricep/knee strengthening exercises.

Mechanical Interventions

The groups agree that patellar taping can be effective in relieving pain and improving function. Refer to Areas of Difference below for recommendations regarding other mechanical interventions.

Oral Medications

Both groups agree that acetaminophen and NSAIDs are appropriate medications for relieving pain and improving physical function in OA. SMOH recommends that NSAIDS be considered only if the patient is not responding to acetaminophen; AAOS does not make this distinction. SMOH emphasizes that all NSAIDs (including both COX-2 selective and non-selective NSAIDs) should be prescribed at the lowest possible dose and for the shortest possible duration. There is overall agreement that COX-2 inhibitors may be better tolerated than non-selective NSAIDs in patients at increased gastrointestinal risk (age $\geq$ 60 years, a history of adverse GI events [e.g., GI bleeding, peptic ulcer disease, etc.], concomitant corticosteroid use). SMOH warns, however, that although COX-2 inhibitors have relatively lower risk of gastroduodenal adverse effects, long-term use has been associated with myocardial and cerebral infarction. The groups further agree that patients at increased GI risk taking non-selective NSAIDs should receive concomitant gastro-protective therapy.

SMOH also provides guidance specific to individual NSAIDs, including celecoxib, etoricoxib, meloxicam and nimesulide.

Topical Medications

The groups agree that topical NSAIDs can be considered for relief of pain due to OA. SMOH stated that topical capsaicin may also be considered for this purpose.

Intra-Articular Injections

Both groups address intra-articular corticosteroid and hyaluronan injections, and agree that intra-articular corticosteroid injections are an appropriate intervention for short-term pain relief for patients with symptomatic OA of the knee. According to SMOH, intra-articular injections should only be considered if general measures and systemic therapies have failed or are contraindicated. Refer to Areas of Difference for additional information.

Surgery

The AAOS guideline covers treatment of OA of the knee in adults up to, but not including, knee replacement. With regard to non-arthroplastic surgical interventions, they note that arthroscopic partial meniscectomy or loose body removal is an option in patients with symptomatic OA of the knee who also have primary signs and symptoms of a torn meniscus and/or a loose body. They also

note that realignment osteotomy is an option in active patients with symptomatic unicompartmental OA of the knee with malalignment.

SMOH does not provide specific surgical recommendations, but recommends referral to an orthopedic surgeon when conservative management has failed. They add that for patients who are eligible for surgery, both unicompartmental and total knee arthroplasty are cost-effective in terms of quality of life gain.

Areas of Difference

Physical Activity and Weight Loss

SMOH recommends certain physical activity interventions that AAOS does not address, one of which is regular water-based or pool exercises. According to SMOH, they reduce pain and improve physical function. Another intervention recommended by SMOH is manual therapy, the use of specific hands-on techniques applied to soft tissue and joint structures around the knee, together with an exercise program, to improve knee function and pain relief.

Mechanical Interventions

According to SMOH, lateral wedge insoles (tilt angle of 8.5 to 11 degrees) should be used to provide pain relief for OA of the knee with medial OA symptoms. AAOS, in contrast, suggests that lateral heel wedges not be prescribed for patients with symptomatic medial compartmental OA of the knee.

Moreover, SMOH states that valgus knee brace and knee sleeves may be used to provide significant improvement in functional tasks and unloading of varus deformity. AAOS, in contrast, was unable to recommend for or against the use of braces with either a valgus or varus directing force.

Other Non-Pharmacologic Interventions

Recommendations regarding acupuncture differ. While AAOS states that it is unable to recommend for or against the use of acupuncture as an adjunctive therapy for pain relief in patients with symptomatic OA of the knee, SMOH notes that needle electro-acupuncture may be used as an adjunct for symptomatic relief of pain and improvement of knee function.

SMOH provides recommendations for non-pharmacologic interventions not addressed by AAOS. According to SMOH, TENS should be used to provide short-term relief of OA of the knee pain, reduce stiffness and improve knee range of motion, with effects lasting for 4 weeks. SMOH also states that interferential current therapy may be used to reduce pain and increase in knee range of motion for OA of the knee patients. AAOS does not address TENS or interferential current therapy.

Glucosamine/Chondroitin

Recommendations regarding the use of glucosamine and/or chondroitin differ. AAOS recommends that glucosamine and/or chondroitin sulfate or hydrochloride not be prescribed for patients with symptomatic OA of the knee. SMOH, in

contrast, states that patients who have failed to respond to analgesics and nonpharmacologic measures and want to try glucosamine may be given glucosamine sulphate 1500 mg once daily.

Intra-Articular Injections

Recommendations differ with regard to intra-articular hyaluronic acid (viscosupplementation). While AAOS could not recommend for or against the use of intra-articular hyaluronic acid, SMOH states that it can be an appropriate pain-relief intervention in patients in whom other treatments have failed or are contraindicated. They add that it is effective with beneficial effects on pain, function and patient global assessment.

COMPARISON OF RECOMMENDATIONS	
NON-PHARMACOLOGIC INTERVENTIONS **Abbreviations** **Back to TOC**	
Physical Activity and Weight Loss	
AAOS (2008)	**Patient Education and Lifestyle Modification** The authors suggest patients with symptomatic OA of the knee be encouraged to participate in self-management educational programs such as those conducted by the Arthritis Foundation, and incorporate activity modifications (e.g., walking instead of running; alternative activities) into their lifestyle. (**Grade B, Level II**) Regular contact to promote self-care is an option for patients with symptomatic OA of the knee. (**Grade C, Level IV**) The authors recommend patients with symptomatic OA of the knee, who are overweight (as defined by a BMI>25), should be encouraged to lose weight (a minimum of five percent [5%] of body weight) and maintain their weight at a lower level with an appropriate program of dietary modification and exercise. (**Grade A, Level I**) **Rehabilitation** The authors recommend patients with symptomatic OA of the knee be encouraged to participate in low-impact aerobic fitness exercises. (**Grade A, Level I**) Range of motion/flexibility exercises are an option for patients with symptomatic OA of the knee. (**Grade C, Level V**) The authors suggest quadriceps strengthening for patients with symptomatic OA of the knee. (**Grade B, Level II**)

SMOH (2007)	**<u>Non-Pharmacological Management</u>** **Exercise** **A** - Regular knee strengthening and aerobic exercises should be encouraged and taught to patients with OA of the knees, as these improve functional ability, aerobic and endurance capacity and reduce knee pain. (**Grade A, Level 1+**) **Weight Reduction** **A** - Weight loss can result in significant changes in knee joint biomechanics with improved knee function for stair climbing and other daily activities. It is most effectively achieved by a combination of exercise and dietary control. (**Grade A, Level 1+**) **Hydrotherapy** **A** - Regular water-based exercise or exercises in the pool are recommended as these exercises reduce pain and improve physical function in patients with OA of the knees. (**Grade A, Level 1++**) **Manual Therapy** **A** - Manual therapy applied to the knee together with an exercise programme may be used to improve knee function and pain relief for patients with OA of the knee. (**Grade A, Level 1+**)
Mechanical Interventions	
AAOS (2008)	**Mechanical Interventions** The authors suggest patients with symptomatic OA of the knee use patellar taping for short term relief of pain and improvement in function. (**Grade B, Level II**) The authors suggest lateral heel wedges not be prescribed for patients with symptomatic medial compartmental OA of the knee. (**Grade B, Level II**) The authors are unable to recommend for or against the use of a brace with a valgus directing force for patients with medial uni-compartmental OA of the knee. (**Inconclusive, Level II**) The authors are unable to recommend for or against the use of a brace with a varus directing force for patients with lateral uni-compartmental OA of the knee. (**Inconclusive, Level V)**

SMOH (2007)	**Taping** **A** - Taping may be used to shift the patella medially and provide effective relief of pain in OA of the knee. (**Grade A, Level 1++**) **Braces and Wedges** **B** - Lateral wedge insoles (tilt angle of 8.5 to 11 degrees) should be used to provide pain relief for OA of the knee with medial OA symptoms. (**Grade B, Level 1+**) **B** - Valgus knee brace and knee sleeves may be used to provide significant improvement in functional tasks and unloading of varus deformity. (**Grade B, Level 1+**) Lateral wedge insoles provide significant pain relief for OA of the knee with varus deformity, while protective knee sleeve and Valgus knee braces can provide significant improvement during functional tasks (stair climbing, 6-minute walk test) by providing improved stability, proprioception and mechanical re-alignment of knee mechanics.
Other Non-Pharmacologic Interventions	
AAOS (2008)	**Complementary and Alternative Therapy** The authors are unable to recommend for or against the use of acupuncture as an adjunctive therapy for pain relief in patients with symptomatic OA of the knee. (**Inconclusive, Level I**) **Needle Lavage** The authors suggest that needle lavage not be used for patients with symptomatic OA of the knee. (**Grade B, Level II**)
SMOH (2007)	**TENS** **B** - TENS, in the form of strong burst mode with high frequency, should be used to provide short-term relief of OA of the knee pain, reduce stiffness and improve knee range of motion, with effects lasting for 4 weeks. (**Grade B, Level 1+**) **Interferential Current Therapy** **B** - Interferential current may be used to reduce pain and increase in knee range of motion for OA of the knee patients. (**Grade B, Level 1+**)

	Other Treatment Modalities • Thermal therapy, especially heat, has a long traditional and anecdotal history for the relief of pain, muscle soreness, and tightness, and it encourages muscle relaxation. Diathermy or deep heating of tissues and joints is commonly used to reduce pain in osteoarthritis of the knees; however there is only one study that reported significantly reduced pain after 30 sessions of Shortwave diathermy. Superficial heating with infra-red and red laser, twice daily over 10 days, was found to result in reduction of 39% on pain scale with pain relief lasting for 4 months. • Similarly, ice therapy is also found to be statistically beneficial to reduce pain hence improve quadricep strength in patients with osteoarthritis of the knee. **Other Alternative Therapies** **A** - Needle electro-acupuncture may be used as an adjunct for symptomatic relief of pain and improvement of knee function. (**Grade A, Level 1++**)
PHARMACOLOGIC INTERVENTIONS **Abbreviations** **Back to TOC**	
Oral Medications	
AAOS (2008)	**Pain Relievers** The authors suggest patients with symptomatic OA of the knee receive one of the following analgesics for pain unless there are contraindications to this treatment: • Acetaminophen [not to exceed 4 grams per day] • NSAIDs (**Grade B, Level II**) The authors suggest patients with symptomatic OA of the knee and increased GI risk (Age $\geq$ 60 years, comorbid medical conditions, history of peptic ulcer disease, history of GI bleeding, concurrent corticosteroids and/or concomitant use of anticoagulants) receive one of the following analgesics for pain: • Acetaminophen [not to exceed 4 grams per day] • Topical NSAIDs • Nonselective oral NSAIDs plus gastro-protective agent • COX-2 inhibitors

	(**Grade B, Level II**)
SMOH (2007)	**<u>Analgesics in OA of the Knees</u>** **Oral Paracetamol** **A** - Paracetamol (acetaminophen) should be considered as the first line of treatment for relieving pain and improving physical functioning in OA (Towheed et al., 2003; Jordan et al., 2003; Altman et al., 2000). (**Grade A, Level 1+**) **NSAIDs** **A** - Non-selective NSAIDs should be used for the acute relief of pain and improvement in function for as short a period as possible. The benefits of using NSAIDs should be weighed against the potential adverse reactions, especially with long-term use, in individuals at risk (Watson et al., 2000). (**Grade A, Level 1+**) **GPP** - The selection of a NSAID for prescription for OA knee should be based upon relative safety, patient acceptability and cost effectiveness. (**GPP**) **GPP** - Patients who develop hypersensitivity reactions to NSAIDs are usually able to tolerate COX-2 selective inhibitors. These should preferably be prescribed following demonstration of tolerance through supervised drug provocation tests. (**GPP**) **A** - Patients with moderately high risk for gastroduodenal bleeds should receive concomitant GPA when using nonselective NSAIDs (Gabriel, Jaakkimainen, & Bombadier, 1991). Risk factors for gastrointestinal complications include (Gabriel, Jaakkimainen, & Bombadier, 1991): • Age greater than 60 years • Previous history of gastrointestinal events (e.g., peptic ulcer disease) • Concomitant corticosteroid use (**Grade A, Level 1+**) **A** - Recommended prophylactic GPA against gastroduodenal ulcers include (Rostom et al., 2002): • Standard dose of proton-pump inhibitors (omeprazole 20 mg once daily) • Misoprostol 400-800 mcg/day • Double dose of H2-receptor antagonists (famotidine 40 mg bd,

ranitidine 300 mg bd)

(**Grade A, Level 1+**)

COX-2 Selective Inhibitors

A - COX-2 selective inhibitors may be used acutely in the reduction of pain from OA of the knees (Bombardier et al., 2000; Silverstein et al., 2000; Schnitzer et al., 2004). Although these drugs have relatively lower risk of gastroduodenal adverse effects, long-term use has been associated with myocardial and cerebral infarction (Bresalier et al., 2005; Solomon et al., 2005; Nussmeier et al., 2005). (**Grade A, Level 1+**)

GPP - When NSAIDs (including both COX-2 selective and non-selective NSAIDs) are needed for the management of an individual patient, they should be prescribed at the lowest effective dose. The duration of treatment should be periodically reviewed and kept as short as possible. (**GPP**)

GPP - All NSAIDs should not be prescribed in patients who have recently undergone CABG surgery and revascularization procedures. (**GPP**)

GPP - The benefits and risks of celecoxib and etoricoxib should be carefully assessed before they are prescribed to any individual patient, taking into consideration other available therapeutic options. (**GPP**)

GPP - Celecoxib or etoricoxib should not be prescribed for patients with established ischaemic heart disease, stroke or congestive heart failure. (**GPP**)

GPP - Caution should be exercised when prescribing celecoxib or etoricoxib to patients who have the following risk factors: hypertension, hyperlipidaemia, diabetes and smoking, as well as patients with peripheral arterial disease. (**GPP**)

GPP - Etoricoxib should not be prescribed for patients with hypertension whose blood pressure has not been adequately controlled. (**GPP**)

NSAIDs with Preferential COX-2 Inhibition

A - Meloxicam and nimesulide are two NSAIDs with preferential COX-2 inhibition which may be used in the short term relief of pain from OA of the knees (Bianchi & Broggini, 2003; Herrera & Gonzalez, 2003; Chang et al., 2001; Hawkey et al., 1998). (**Grade A, Level 1+**)

	Tramadol **A**- Tramadol may be used as an alternative to NSAIDs for pain relief and improvement in physical functioning, especially where the risks of adverse effects from NSAIDs outweigh the benefits (Cepeda et al., 2006; Babul et al., 2004). (**Grade A, Level 1+**) **Oral Corticosteroids** **GPP** - Oral corticosteroids are not indicated for management of knee OA. (**GPP**) **Cost-Effectiveness Issues** **GPP** - Pain medications are important in managing OA symptoms and should be used concurrently with nutritional, physical, and educational interventions. Doctors should consider efficacy, adverse side effects, dosing frequency, and cost to the patient when recommending OA treatments. (**GPP**) **C** - For mild to moderate OA pain, paracetamol is the drug of choice as it is cost-effective and has minimal side-effects. In treating moderate to severe OA pain, the use of NSAIDs and COX-2 specific inhibitors (for a patient who is at high risk of adverse upper gastrointestinal events) should be considered only if the patient is not responding to paracetamol (Kamath et al., 2003). (**Grade C, Level 2+**)
Topical Medications	
AAOS (2008)	**Pain Relievers** The authors suggest patients with symptomatic OA of the knee and increased GI risk (Age $\geq$ 60 years, comorbid medical conditions, history of peptic ulcer disease, history of GI bleeding, concurrent corticosteroids and/or concomitant use of anticoagulants) receive one of the following analgesics for pain: • Acetaminophen [not to exceed 4 grams per day] • Topical NSAIDs • Nonselective oral NSAIDs plus gastro-protective agent • Cyclooxygenase-2 inhibitors (**Grade B, Level II**)
SMOH (2007)	**Topical NSAIDs and Medications** **A** - Topical NSAIDs can be considered for the short-term symptomatic relief of pain in OA. Side effects of topical NSAIDs are

	usually minor. (**Grade A, Level 1+**) **A** - Topical capsaicin may also be considered in relieving pain due to OA. Transient local burning sensation may occur at the site of application. (**Grade A, Level 1+**)
Glucosamine/Chondroitin	
AAOS (2008)	**Complementary and Alternative Therapy** The authors recommend glucosamine and/or chondroitin sulfate or hydrochloride not be prescribed for patients with symptomatic OA of the knee. (**Grade A, Level I**)
SMOH (2007)	**<u>Glucosamine/Chondroitin in the Treatment of OA</u>** **Efficacy** Neither glucosamine hydrochloride nor chondroitin sulfate alone has been shown to be more efficacious than placebo for the treatment of knee pain. **B** - Patients who have failed to respond to analgesics and nonpharmacologic measures and want to try glucosamine may be given glucosamine sulphate 1500 mg once daily as pharmacologic studies suggest that maximal benefit is better achieved at this dose (Persiani et al., 2005). (**Grade B, Level 2++**) **B** - Patients who are already taking glucosamine and report improvement in symptoms may discontinue after a period of 6 months as evidence suggests that regular use for more than 6 months is no more effective than placebo in the relief of joint pain (Cibere et al., 2004). (**Grade B, Level 1+**) **GPP** - Patients allergic to shellfish should be warned about possible allergic reactions to glucosamine. (**GPP**)
Intra-Articular Injections	
AAOS (2008)	**Intra-Articular Injections** The authors suggest intra-articular corticosteroids for short-term pain relief for patients with symptomatic OA of the knee. (**Grade B, Level II**) The authors cannot recommend for or against the use of intra-articular hyaluronic acid for patients with mild to moderate symptomatic OA of the knee. (**Inconclusive, Level I and II**)

SMOH (2007)	**Intra-articular Injections** **Viscosupplementation** **B** - Viscosupplementation can be used for treatment of OA of the knee, where general measures or systemic therapies have failed or are contraindicated. It is effective with beneficial effects on pain, function and patient global assessment; and at different post injection periods but especially at the 5 to 13 week post injection period when compared with placebo (Bellamy et al., 2006). (**Grade B, Level 1+**) **GPP** - In Singapore, data on effectiveness are too limited to allow any conclusions to be drawn regarding cost-effectiveness of viscosupplementation. However, in view of the relative high cost of viscosupplementation and its comparable efficacy with other forms of systemic intervention, it should be considered only if general measures and systemic therapies have failed or are contraindicated. (**GPP**) Hyaluronic acid products had more prolonged effects than intra-articular corticosteroids. Sample-size restrictions preclude any definitive comment on the safety of the hyaluronic acid class of products. However, within the constraints of the trial designs employed, no major safety issues were detected. **Intra-Articular Corticosteroid** **B** - In patients with knee OA who are symptomatic despite general measures and systemic therapies, evidence supports short term (up to two weeks) improvement of symptoms from intra-articular corticosteroid injection (Arroll & Goodyear-Smith, 2004). (**Grade B, Level 1**) **GPP** - Regular use of intra-articular steroids is not recommended for OA of the knees in the general practice setting. (**GPP**)
SURGICAL INTERVENTION Abbreviations Back to TOC	
AAOS (2008)	**Note**: This guideline covers treatment of OA of the knee in adults up to, but not including, knee replacement. **Surgical Intervention** The authors recommend against performing arthroscopy with debridement or lavage in patients with a primary diagnosis of

	symptomatic OA of the knee. (**Grade A, Level I and II**) Arthroscopic partial meniscectomy or loose body removal is an option in patients with symptomatic OA of the knee who also have primary signs and symptoms of a torn meniscus and/or a loose body. (**Grade C, Level V**) The authors cannot recommend for or against an osteotomy of the tibial tubercle for patients with isolated symptomatic patello-femoral OA. (**Inconclusive, Level V**) Realignment osteotomy is an option in active patients with symptomatic unicompartmental OA of the knee with malalignment. (**Grade C, Level IV and V**) The authors suggest against using a free-floating interpositional device for patients with symptomatic unicompartmental OA of the knee. (**Grade B, Level IV**)
SMOH (2007)	**Surgery** **GPP** - A referral to the orthopaedic surgeon should be made when conservative management mentioned previously has failed. (**GPP**) **Cost-Effectiveness Issues** **C** - For patients who have failed medical therapy and who are suitable for surgical interventions, both unicompartmental and total knee arthroplasty are cost effective in terms of quality of life gain (Soohoo et al., 2006; Slover et al., 2006; Lavernia, Guzman, & Gachupin-Garcia, 1997). (**Grade C, Level 2+**) **Note**: Refer to the original guideline document for diagnosis-specific surgical options.

STRENGTH OF EVIDENCE AND RECOMMENDATION GRADING SCHEMES **Abbreviations** **Back to TOC**	
AAOS (2008)	**Levels of Evidence for Primary Research Question[1]**

	Types of Studies		
	Therapeutic Studies Investigating the results of treatment	**Prognostic Studies** Investigating the effects of a patient	**Diagnostic Studies** Investigating a diagnostic test

	characteristic on the outcome of disease		
Level I	• High quality randomized trial (RCT) with statistically significant difference but narrow confidence intervals, • Systematic Review[2] of Level I RCTs (and study results were homogenous[3])	• High quality prospective study[4] (all patients were enrolled at the same point in their disease with ≥80% follow-up of enrolled patients) • Systematic review[2] of Level I studies	• Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference "gold" standard) • Systematic review[2] of Level I studies
Level II	• Lesser quality RCT (e.g., <80% follow-up, no blinding, or improper randomization) • Prospective[4] comparative study[5] • Systematic review[2] of Level II studies or Level I studies with inconsistent results	• Retrospective[6] study • Untreated controls from an RCT • Lesser quality prospective study (e.g., patients enrolled at different points in their disease or <80% follow-up) • Systematic review[2] of Level II studies	• Development of diagnostic criteria on consecutive patients (with universally applied reference "gold" standard) • Systematic review[2] of Level II studies
Level III	• Case control study[7] • Retrospective[6] comparative study[5] • Systematic review[2] of Level III studies	• Case control study[7]	• Study of non-consecutive patients; without consistently applied reference "gold" standard • Systematic review[2] of Level III studies

Level IV	Case Series[8]	Case Series	• Case-control study • Poor reference standard
Level IV	Expert Opinion	Expert Opinion	Expert Opinion

1. A complete assessment of quality of individual studies requires critical appraisal of all aspects of the study
2. A combination of results from two or more prior studies.
3. Studies provided consistent results.
4. Study was started before the first patient enrolled.
5. Patients treated one way (e.g., cemented hip arthroplasty) compared with a group of patients treated in an hip arthroplasty) at the same institution.
6. The study was started after the first patient enrolled.
7. Patients identified for the study based on their outcome, called "cases" (e.g., failed total hip arthroplasty) a not have outcome, called "controls" (e.g., successful total hip arthroplasty).
8. Patients treated one way with no comparison group of patients treated in another way.

Grading the Recommendations

A: Good evidence (Level I Studies with consistent finding) for or against recommending in

B: Fair evidence (Level II or III Studies with consistent findings) for or against recommen

C: Poor quality evidence (Level IV or V) for or against recommending intervention.

I: There is insufficient or conflicting evidence not allowing a recommendation for or agains

SMOH (2007)

Levels of Evidence

Level	Type of Evidence
1++	High quality meta-analyses, systematic reviews of randomised controlled trials very low risk of bias.
1+	Well conducted meta-analyses, systematic reviews of RCTs or RCTs with a low
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.
2++	High quality systematic reviews of case control or cohort studies. High quality studies with a very low risk of confounding or bias and a high probability that causal.
2+	Well conducted case control or cohort studies with a low risk of confounding o probability that the relationship is causal.

2-	Case control or cohort studies with a high risk of confounding or bias and a sig relationship is not causal.
3	Non-analytic studies (e.g., case reports, case series).
4	Expert opinion.

Grades of Recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, dir target population, and demonstrating overall consistency of results.
B	A body of evidence including studies rated as 2++, directly applicab population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+.
C	A body of evidence including studies rated as 2+, directly applicable population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++.
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+.
GPP (good practice points)	Recommended best practice based on the clinical experience of the group.

COMPARISON OF METHODOLOGY ***Click on the links below for details of guideline development methodology***	
AAOS METHODOLOGY (2008)	**SMOH METHODOLOGY (2007)**
Both groups performed searches of electronic databases to collect the evidence; AAOS also performed hand-searches of published literature (both primary and	

secondary sources). AAOS provides a description of methods used to collect and select the evidence, which includes the names of the electronic databases searched (Cochrane and PubMed), the date up to which evidence was searched for (February 22nd, 2008), inclusion/exclusion criteria applied, the number of source documents, and search strategies used.

To assess the quality and strength of the evidence, both groups used weighting according to a rating scheme and provide the scheme. AAOS and SMOH performed a review of published meta-analyses to analyze the evidence, as well as a systematic review (AAOS' systematic review incorporated evidence tables). AAOS also performed a meta-analysis of randomized controlled trials, and it provides a description of methods used to analyze the evidence.

With regard to cost-analyses, AAOS did not perform a formal cost analysis and did not review published cost analyses. SMOH, in contrast, reviewed published cost analyses and summarized cost-effectiveness issues in the "Major Recommendations" field as well as in the original guideline document.

Both groups employed expert consensus (AAOS specifies the nominal group technique) to formulate their recommendations. The strength of the recommendations was graded by both groups, and the rating schemes are provided. Peer review was used as a method of guideline validation by both groups; AAOS specifies that it used internal and external peer review. AAOS also provides a description of the peer review process.

SOURCE(S) OF FUNDING
Abbreviations
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AAOS (2008)	This guideline and the systematic review upon which it is based were funded by the AAOS, with additional funding received from the Arthroscopy Association of North American (AANA) and the American Orthopedic Society of Sports Medicine (AOSSM).
SMOH (2007)	Singapore Ministry of Health

BENEFITS AND HARMS
Abbreviations
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Benefits

AAOS (2008)	Effective treatment of OA of the knee in adults
SMOH (2007)	• Appropriate management of OA of the knees • Reduction in pain and improved physical functioning
Harms	
AAOS (2008)	Individuals with OA of the knee often complain of joint pain, stiffness, and functional deficits. The aim of treatment is pain relief and improvement or maintenance of the patient's functional status. Long term results were often not available and adverse events varied by study (frequently they were not reported) in the literature available for this guideline. Most treatments are associated with some known risks, especially invasive and operative treatments. Therefore, discussion of available treatments and procedures applicable to the individual patient rely on mutual communication between the patient and physician, weighing the potential risks and benefits for that patient.
SMOH (2007)	**Oral Paracetamol** Gastrointestinal discomfort was more frequent with NSAIDs than with paracetamol. **Non-Selective NSAIDs** • Gastrointestinal (gastroduodenal perforations, ulcers and bleeds, small bowel perforations) • Renal (hyperkalaemia, hypertension, oedema, acute renal insufficiency) • Hypersensitivity reactions including periorbital angioedema, urticaria, rhinitis or attacks of asthma Emerging evidence suggests that there are cardiovascular risks associated with non-selective NSAIDs as well, although this could not be conclusively demonstrated in a recent meta-analysis. **COX-2 Selective Inhibitors** • Supervised drug provocation tests by specialists trained in allergy/immunology are recommended before using COX-2 inhibitors in NSAID-sensitive individuals. • Although these drugs have relatively lower risk of gastroduodenal adverse effects, long-term use has been associated with myocardial and cerebral infarction. • The COX-2 selective inhibitors have recently been found to be associated with increased cardiovascular events, leading to the withdrawal of rofecoxib in Singapore in October 2004. • In addition to the increased cardiovascular risks, reports of severe

	cutaneous reactions (Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis) among patients taking valdecoxib resulted in the drug being removed from the market in several countries including Singapore in April 2005. • All NSAIDs should not be prescribed in patients who have recently undergone CABG surgery and revascularization procedures. • Celecoxib or etoricoxib should not be prescribed for patients with established ischaemic heart disease, stroke or congestive heart failure. • Caution should be exercised when prescribing celecoxib or etoricoxib to patients who have the following risk factors: hypertension, hyperlipidaemia, diabetes and smoking, as well as patients with peripheral arterial disease. • Etoricoxib should not be prescribed for patients with hypertension whose blood pressure has not been adequately controlled. **NSAID with Preferential COX-2 Inhibitors** Although it is indicated for the short-term relief of joint pain, there have been reports of elevated liver enzymes and hepatitis. **Tramadol** Nausea/giddiness **Glucosamine/Chondroitin** Patients allergic to shellfish should be warned about possible allergic reactions to glucosamine. **Viscosupplementation** Viscosupplements were comparable in efficacy to systemic forms of active intervention (e.g., NSAIDs), with more local reactions (post injection inflammation) but fewer systemic adverse events. **Topical NSAIDs and Medications** Topical capsaicin may cause local burning sensation, and this may limit its use in some patients.

CONTRAINDICATIONS **Abbreviations** **Back to TOC**	
AAOS	Contraindications vary widely based on the treatment administered.

(2008)	Therefore, discussion of available treatments and procedures applicable to the individual patient rely on mutual communication between the patient and physician, weighing the potential risks and benefits for that patient.
SMOH (2007)	None provided

Abbreviations
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AAOS, American Academy of Orthopaedic Surgeons

CABG, coronary artery bypass graft

COX-2, cyclooxygenase-2

DJD, degenerative joint disease

GI, gastrointestinal

GPA, gastroprotective agents

NSAID, nonsteroidal anti-inflammatory drug

OA, osteoarthritis

OT, occupational therapy

PT, physical therapy

SMOH, Singapore Ministry of Health

TENS, transcutaneous electrical nerve stimulation

Internet citation: National Guideline Clearinghouse (NGC). Guideline synthesis: Management of osteoarthritis of the knee. In: National Guideline Clearinghouse (NGC) [website]. Rockville (MD): 2009 Jun. [cited YYYY Mon DD]. Available: http://www.guideline.gov.

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